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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/786,533	01/21/1997	MARCUS A. HORWITZ	120-243	5368

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/786,533	Horwitz et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *3, 8, and 28* is/are allowed.

6) ☒ Claim(s) *1, 2, 4-7, and 9-27* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Claims 1-28 are pending and examined on the merits.

2. As the SEQ ID NO:104-138 do not appear in the '842 or '946 application the priority date of claims 13, 16, 19 and 22, drawn to SEQ ID NO:104, 106, 107, 110, 114, 115, 118, 120, 122, 123, 124, 126, 127, 134, 135, 136 and 138 will be that of the instant application, filed 1/21/97.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 26 is rendered vague and indefinite in the recitation of pSMT3 as the sole designation for the claimed vector. The use of laboratory designations only to identify a particular vector renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct vectors. Amendment of the claims to include the depository accession number of a cell line producing the vector, or amendment of the claims to include a SEQ ID NO: is suggested.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

6. Claim 11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Horwitz (US 5,108,745) as evidenced by Kapoor et al (US 5,330,754). Claim 11 is drawn in part to a vaccinating agent comprising at least one immunodominant epitope selected from the group consisting of M tuberculosis 12, 14, and 71 KD antigens. Claim 11 is drawn to a method of immunizing a host comprising administering the vaccinating agent of claim 11. Horwitz teaches a method for immunizing a host comprising the administration of M tuberculosis extracellular proteins as a vaccinating agent. Kapoor et al discloses the 12, 14, and 71 KD antigens of M tuberculosis as immunodominant antigens which are secreted molecules.

7. Claims 11-13, and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Horwitz (US 5,108,745) as evidenced by Borremans (Infection and Immunity, 1989, Vol. 57, pp. 3123-3130). Claims 12, 18 and 11 in part and 17 in part are drawn to a vaccinating agent comprising at the 32A KD antigen of M tuberculosis. Claims 13 and 19 are drawn to the 32A KD antigen of M tuberculosis comprising the amino acid sequences of SEQ ID NO:104, 106, 107, 110, 114, 115, 118, 120, 122, 123, 124, 126, 127, 134, 135, 136 and 138. Claim 18 is drawn to a method of immunizing a host comprising administering the vaccinating agent of claim 17. Horwitz teaches a method for immunizing a host comprising the administration of M tuberculosis extracellular proteins as a vaccinating agent. Borremans teaches that the 32 KD antigen is an immunodominant antigen which is secreted and therefore a extracellular protein. As the recited SEQ ID NO: are fragments of the 32A KD antigen, and claims 13 and 19 are directed to proteins comprising the recited SEQ ID NO, the claims read on the full length 32A KD antigen, and are thus anticipated by Horwitz as evidenced by Borremans.

8. Claims 13 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Content et al (US 5,916,558). Claim 13 is drawn in part to a vaccinating agent comprising the 32A KD antigen of M tuberculosis having the amino acid sequences of SEQ ID NO:104 and 138. Claim 19 is drawn in part to a method of vaccinating a host comprising administering the 32A KD antigen of M tuberculosis having the amino acid sequences of SEQ ID NO:104 and 138. Content

et al disclose a method of vaccinating for M tuberculosis comprising administering an antigen comprising the vaccinating agent of SEQ ID NO:4 (Sequence 25) and SEQ ID NO:138 (Sequence 29).

9. Claims 11-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Content et al (EP 419,355) as evidenced by Accession Numbers AAR11298 and AAR11302. Claims 11 in part, and 12 are drawn to a vaccinating agent comprising the 32A KD antigen of M tuberculosis. Claim 13 specifies the 32 KD antigen having the amino acid sequence of SEQ ID NO:104 and 138. Claim 14 in part, and 15 are drawn to an immunodiagnostic agent comprising the 32A KD antigen of M tuberculosis. Claim 16 specifies the 32 KD antigen having the amino acid sequence of SEQ ID NO:104 and 138. Claims 17 in part and 18 are drawn to a method of immunizing a host comprising the administration of the vaccinating agent of claims 6 and 7. Claims 20 in part, 21 and 22 are drawn to a method of detecting an immune response comprising the use of the immunodiagnostic reagents of claims 14-16. Claims 23-25 are drawn to a process of producing said vaccinating agent and immunodiagnostic agent by a recombinant method of transforming a host cell with a vector. Content et al disclose a method of vaccinating an individual and a method of detecting an immune response, both methods comprising the use of the 30-32KD antigen complex of M tuberculosis and immunodominant fragments thereof. Content et al disclose 32KD immunodominant antigen fragments as peptide comprising SEQ ID NO:104 and 138. Content et al disclose the recombinant production of the antigenic peptides.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 4, 6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horwitz (US 5,108,745) as evidenced by Kapoor et al (US 5,330,754) in view of either of Yoshimoto et al (US 4,789,658) or Roskam et al (US 5,417,970) and what is well known in the art as exemplified by Paul (Immunology, 1993, (text) pp. 1327-1328). Claims 1, in part, and 4 are drawn to a vaccinating agent comprising an abundant extracellular product of M. Tuberculosis and Il-12 as an adjuvant. Claims 6 and 9 are drawn to a method of immunizing an animal comprising administering the vaccinating agent of claims 1 and 4. For the reasons stated in paragraph 4 above, Horwitz teaches the a method of vaccinating an individual comprising the administration of an extracellular product of M tuberculosis. Horowitz does not teach a vaccinating agent comprising Il-12 as adjuvant. It is well known in the art that adjuvant are useful for immunopotentiation of vaccines as taught by Paul. Yoshimoto et al and Roskam et al teach the use of Il-1 as a vaccine adjuvant. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the abundant extracellular products of M tuberculosis and Il-12 in a vaccine used for a method of immunizing an animal. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Paul on the greater immunogenicity of vaccines when formulated with adjuvant and the teachings of Yoshimoto et al and Roskam et al on the efficacy of Il-12 as an adjuvant.

12. Claims 1, 2, 4, 6, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horwitz (US 5,108,745) as evidenced by Borremans (Infection and Immunity, 1989, Vol. 57, pp. 3123-3130) in view of either of Yoshimoto et al (US 4,789,658) or Roskam et al (US 5,417,970) and what is well known in the art as exemplified by Paul (Immunology, 1993, (text) pp. 1327-1328). Claims 1, in part, 2 and 4 are drawn to a vaccinating agent comprising an the 32KD antigen of M tuberculosis and Il-12 as an adjuvant. Claims 6, 7 and 9 are drawn to a method of immunizing an animal comprising administering the vaccinating agent of claims 1, 2 and 4. For the reasons stated in paragraph 5 above, Horwitz teaches the a method of vaccinating an individual comprising the administration of the 32 KD antigen of M. Tuberculosis. Horowitz does not teach a vaccinating agent comprising Il-12. It is well known in the art that adjuvant are useful for immunopotentiation of vaccines as taught by Paul. Yoshimoto et al and Roskam et al teach the use of Il-12 as a vaccine adjuvant. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine 32 KD antigen of M tuberculosis and Il-12 in a vaccine used for a method of immunizing an animal. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Paul on the greater immunogenicity of vaccines when formulated with adjuvant and the teachings of Yoshimoto et al and Roskam et al on the efficacy of Il-12 as an adjuvant.

13. Claim 1, 2, 4, 6, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Content et al (EP 419,355) in view of either of Yoshimoto et al (US 4,789,658) or Roskam et al (US 5,417,970) and what is well known in the art as exemplified by Paul (Immunology, 1993, (text) pp. 1327-1328). The embodiments of claims 1, 2, 4, 6, 7 and 9 are listed in the above paragraph. For the reasons stated in paragraph 7, supra, Content et al teach a method of vaccinating an individual comprising the administration of the 32 KD antigen of M. Tuberculosis. Content et al do not teach a vaccinating agent comprising Il-12. It is well known in the art that adjuvant are useful for immunopotentiation of vaccines as taught by Paul. Yoshimoto et al and Roskam et al teach the use of Il-12 as a vaccine adjuvant. It would have

been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine 32 KD antigen of M tuberculosis and Il-12 in a vaccine used for a method of immunizing an animal. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Paul on the greater immunogenicity of vaccines when formulated with adjuvant and the teachings of Yoshimoto et al and Roskam et al on the efficacy of Il-12 as an adjuvant.

14. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horwitz (US 5,108,745) as evidenced by Kapoor et al (US 5,330,754) in view of Kaslow et al (US 5,217,898) and what is well known in the art as exemplified by Paul (Immunology, 1993, (text) pp. 1327-1328). Claim 1, in part, is drawn to a vaccinating agent comprising an abundant extracellular product of M. Tuberculosis and MF59 as an adjuvant. Claim 6 id drawn to a method of immunizing an animal comprising administering the vaccinating agent of claim 1. For the reasons stated in paragraph 4, Horwitz teaches the a method of vaccinating an individual comprising the administration of an extracellular product of M tuberculosis. Horowitz does not teach a vaccinating agent comprising MF59 as adjuvant. It is well known in the art that adjuvant are useful for immunopotentiation of vaccines as taught by Paul. Kaslow et al teach MF59 as a vaccine adjuvant. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the abundant extracellular products of M tuberculosis and MF59 in a vaccine used for a method of immunizing an animal. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Paul on the greater immunogenicity of vaccines when formulated with adjuvant and the teachings of Kaslow et al et al on the efficacy of MF59 as an adjuvant.

15. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horwitz (US 5,108,745) as evidenced by Borremans (Infection and Immunity, 1989, Vol. 57, pp. 3123-3130) in view of Kaslow et al (US 5,217,898) and what is well known in the art as exemplified by Paul (Immunology, 1993, (text) pp. 1327-1328). Claim 1, in part, is drawn to a vaccinating

agent comprising an the 32KD antigen of M tuberculosis and MF59 as an adjuvant. Claims 6 is drawn to a method of immunizing an animal comprising administering the vaccinating agent of claim 1 For the reasons stated in paragraph 5 above, Horwitz teaches the a method of vaccinating an individual comprising the administration of the 32 KD antigen of M. Tuberculosis. Horowitz does not teach a vaccinating agent comprising MF59. It is well known in the art that adjuvant are useful for immunopotentiation of vaccines as taught by Paul. Kaslow et al teach MF59 as a vaccine adjuvant. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine 32 KD antigen of M tuberculosis and MF59 in a vaccine used for a method of immunizing an animal. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Paul on the greater immunogenicity of vaccines when formulated with adjuvant and the teachings of Kaslow et al on the efficacy of MF59 as an adjuvant.

16. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Content et al (EP 419,355) in view of Kaslow et al (US 5,217,898) and what is well known in the art as exemplified by Paul (Immunology, 1993, (text) pp. 1327-1328). The embodiments of claims 1 and 6 are listed in the above paragraph. For the reasons stated in paragraph 7, Content et al teach a method of vaccinating an individual comprising the administration of the 32 KD antigen of M. Tuberculosis. Content et al do not teach a vaccinating agent comprising MF59. It is well known in the art that adjuvant are useful for immunopotentiation of vaccines as taught by Paul. Kaslow et al teach MF59 as a vaccine adjuvant. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine 32 KD antigen of M tuberculosis and MF59 in a vaccine used for a method of immunizing an animal. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Paul on the greater immunogenicity of vaccines when formulated with adjuvant and the teachings of Kaslow et al on the efficacy of MF59 as an adjuvant.

17. Claims 5 and 10 rejected under 35 U.S.C. 103(a) as being unpatentable over either of Horwitz (US 5,108,745) as evidenced by Kapoor et al (US 5,330,754), or Horwitz (US 5,108,745) as evidenced by Borremans (Infection and Immunity, 1989, Vol. 57, pp. 3123-3130) or Content et al (EP 419,355), in view of Kaslow et al (US 5,217,898) and either of Yoshimoto et al (US 4,789,658) or Roskam et al (US 5,417,970). Claim 5 is drawn to the vaccinating agent of claim 1 wherein said adjuvant is a mixture of Il-12 and MF59. Claim 10 is drawn to a method of immunizing a host comprising administering the vaccinating agent of claim 1 wherein the adjuvant is a mixture of Il-12 and MF-59. The instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to produce a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been taught individually in the prior art. Applying the same logic to the instant process claims, given the teaching of the prior art of on the usefulness of Il-12 and MF59 as vaccine adjuvant it would have been obvious to combine both Il-12 and MF59 collectively for the adjuvant formulation because the idea of doing so would have logically followed from their having been individually taught in the prior art to be useful as vaccine adjuvants.

18. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Content et al (EP 419,355), in view of Bloom et al (US 5,504,005). Claim 27 is drawn to the recombinant production of the 32 KD antigen of M tuberculosis. Content et al teach the 32 KD antigen of M tuberculosis and fragments thereof as vaccinating agents. Content et al also teach the recombinant expression of the 32 KD antigen. Content et al do not teach the host cell of M smegmatis. Bloom et al teach the host cell of M smegmatis for the recombinant production of vaccines against M tuberculosis. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the host cell of M smegmatis with the host cell of E. Coli as taught by Content et al. One of ordinary skill in the art would

have been motivated to do so with a reasonable expectation of success by the teachings of Bloom et al on the efficacy of expressing mycobacterium genes in M smegmatis.

Conclusion

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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December 15, 2001

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